CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-658/S-018
19-670/S-018
20-470/S-016
20-641/S-009
20-704/S-008

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

MEETING MINUTES

NDA #:	19-658/S-018, 20-470/S-016, 20-641/S-009, 20-704/S-008, 19-670/S-018
Sponsor:	Schering
Drug Product:	Claritin (loratadine)
Meeting Date:	June 11, 2003 (Teleconference)

Background

On November 13, 2002, Schering committed to two agreements for all loratadine-containing products for post-approval follow-up on hypospadias and use in the 2-5 year old age group. The 2-5 year old age group agreement included tracking adverse event data in an electronic database. When developing this database, Schering had several questions that needed FDA input. These questions were faxed to FDA on March 11, 2003, and are discussed below.

Meeting Attendees

FDA Division of OTC Drug Products

Linda Hu, M.D.	Medical Officer
Elaine Abraham, R.Ph.	Project Manager

Schering

Mary Jane Nehring	Senior Director Marketed Products Support and Training
Beth McKevitt	Research Information Systems
Paul Fallot	Drug Safety Group

Meeting Minutes

The following questions on the Claritin Electronic Database were submitted by Schering and discussed at this meeting.

1. What is the ISR number?

   FDA response: This is an FDA-generated number and should not be included in the electronic database.

2. We are assuming that the Case number corresponds to the Manufacturing Report Number on the MedWatch. Is this correct?

   FDA response: Yes. The sponsor clarified that any follow-up on a case will use the same number.

3. For indication, should we provide the MedDRA term or reported term?

   The sponsor agreed to provide both terms.

4. Since the SP safety system can accommodate many suspect drugs for each patient, we can provide the "main" suspect drug information in the fields listed (i.e. Indication, Suspect Drug, Dose, Duration). Where should we put information for any additional suspect drugs?

   Schering stated that there could be an unlimited number of records because of multiple suspect drugs and doses. They suggest providing a "main" suspect drug.

   FDA response: This is acceptable for now but we may want to revisit this issue after reviewing some of the data collected.

5. The SP safety system can accommodate many Doses and Durations for a given drug. How should we provide this information when a patient is taking a drug with more than one dose?

   FDA response: The sponsor should provide the dose and duration of use at the time of onset of the adverse event.

6. Does "Serious or nonserious" refer to seriousness at the patient level or at the AE level?

   FDA response: We are interested in whether the case was serious and whether there was a death.

7. Since the SP safety system can accommodate many adverse events for each patient, we can provide the expectedness for the primary AE in the "Event expected or unexpected" column. Where should we put expectedness for the additional AEs?

   FDA response: Multiple AEs can be provided on separate rows since the sponsor stated this format would be easier for them to provide. In this case, the expectedness can be provided in a single column.

8. Same question as above for Onset Date.

   FDA response: See answer to Question 7.

9. In the Concomitant Drugs column, should the drugs be comma delimited?

   FDA response: Use separate cells for concomitant medications.

10. Please note that, since a patient can have an unlimited number of AEs, the "row" created for each patient will be quite "wide" if we are to put each AE in a separate column. Is this acceptable and desirable?

    FDA response: See answer to Q7.

11. How should we provide the Age units?

    FDA response: Use decimal years, for example, 4.5 years.

12. How should we provide the Weight units?

    FDA response: Use decimals and identify whether the weight is in kilograms or pounds.

13. Should this database be provided for all patients included in the report or just the 2-5 year old age group?

    FDA response: The database should include all children under 6 years of age.

The Agency and the Sponsor agreed that this format will be used for now but we may want to revisit this issue after reviewing some of the data collected.

Draft by: HFD-560/Abraham/6-18-03
Initialed by: HFD-560/Hu/7-2-03

Final: HFD-560/Abraham/7-8-03

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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Elaine Abraham
7/8/03 11:19:07 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research

MEMORANDUM

DATE: Thursday, November 21, 2002

FROM: Robert J. Meyer, Director, ODE II

TO: **File:** sNDA to 19-658 (s-018), 20-704 (s-008), 20-641 (s-009), 19-670(s-018), 20-470(s-016).
Supplements for the switch to OTC status for the loratadine line of products

SUBJECT: Documentation of ODE II review conclusions

BACKGROUND:
These 5 supplements were submitted by the sponsor with the intent of gaining approval of these applications for nonprescription marketing of Claritin (loratadine) tablets, syrup and Redi-Tabs, as well as Claritin D-12 (loratadine 5 mg/pseudoephedrine 120 mg) and Claritin D-24 (loratadine 10 mg/ pseudoephedrine 240 mg). This memo is to document the review opinions for the Office of Drug Evaluation II. Note that the review of these supplements was a joint effort with the Division of Over-the-Counter Drug Products and ODE V, the latter being primarily responsible for labeling and comprehension study data analysis. This memo is intended to largely focus on the issues of the review primarily addressed by the Division of Pulmonary and Allergy Drug Products and ODE II.

The agency has had both formal and informal communications in recent years with Schering-Plough (along with the sponsors of fexofenadine and ceterizine) encouraging the sponsors to make the Claritin products available OTC. The rationale for this is that the currently marketed OTC antihistamines, while safe and effective, do have the propensity to cause sedation in susceptible individuals which may contribute to impaired driving and other tasks requiring alertness and unfettered motor skills (e.g., operating heavy machinery). Indeed, there is a statement in their labeling warning of these effects. It would appear reasonable, then, from a public health perspective to move the Claritin products to OTC status and thereby offer less sedating alternatives to consumers choosing to self-medicate for seasonal allergies. Claritin without a physician's prescription in most other major countries, including Canada.

Additionally, in 1998 the Agency received a petition from WellPoint (nee Blue Cross/Blue Shield of California) asking the FDA to use its regulatory authority to force the switch of loratadine, fexofenadine and ceterizine to OTC status. Their argument was in part based on a similar public health rationale to that above (albeit not supported by much substantive data), but also seemed to be based on concerns of reimbursement costs for these products as prescription drugs. While that petition has not be definitively answered, it did lead to a joint NDAC/PADAC advisory committee meeting on May 11th, 2001, the abbreviated minutes

of which are in the action package for these supplements. It is already accepted by the FDA that antihistamines themselves are suitable for OTC marketing and that allergic rhinitis is a disease that consumers can self-treat with proper instructions, as evidenced by monograph antihistamines and their attendant labeling. Therefore, the questions to the committee focused on whether there each of these three products, considered separately, were sufficiently safe for OTC marketing for the treatment of allergic rhinitis (i.e., without the intervention of a learned intermediary). The voting was preceded by a presentation from WellPoint and the FDA, the latter of which focused on safety data from the NDAs, the AERS system, from data available from foreign markets where loratadine is OTC and the medical literature. The committee voted 19 yes and 4 opposed for loratadine. Interestingly, at that point, the sponsor spoke passionately against this switch, as proposed by WellPoint.

An additional issue that plays into all of this is that the exclusivity for loratadine expires in December 2002. The agency already has several ANDAs for competing products either under review or tentatively approved. In fact, the agency has three 505(b)(2) applications in house for OTC marketing of loratadine products by competing sponsors. Therefore, even if Schering-Plough persisted in only wanting to market loratadine Rx, the moiety might be moved to OTC status due to other applications proposing such marketing.

These supplements were submitted by Schering-Plough in January of 2002 proposing the switch of all the loratadine products, for all approved age groups and for all approved indications – which includes not only allergic rhinitis, but also hives or chronic idiopathic urticaria (CIU). These supplements have a PDUFA goal date of 11-27-02, several weeks ahead of the patent expiration. It is notable that loratadine is only approved for seasonal allergic rhinitis in the US and not perennial. However, in the OTC antihistamine monographs, no real distinction is made between these entities. Rather, the indication is for "hay fever or other upper respiratory allergies." This statement is arguably broader than seasonal allergic rhinitis, but is appropriately applied to loratadine. However, the hives indication for an oral antihistamine is not a generally accepted indication for OTC use. Further, CIU, the approved Rx indication, is only a subset of hives. Since the considerations for hives were quite different from those related to marketing of Claritin OTC for allergic rhinitis, hives was split off into separate supplements that will be separately addressed.

Clinical:

Please see Dr. Lee's review and Dr. Purucker's memo for detailed discussions. The sponsor has added to prior work undertaken by the FDA in support of answering the WellPoint petition and conducting the May 2001, advisory committee meeting in providing a sufficient argument for making these products available OTC for the treatment of allergic rhinitis. While no drug, including the currently available OTC antihistamines are entirely "safe" in all circumstances and all manners of use, loratadine's safety profile favorably compares to other drugs switched in recent years (e.g., H2-blockers) and compared to the monograph antihistamines. Loratadine does not have the same concern over cardiac repolarization effects and QT prolongation that terfenadine and astemizole had (2 second generation antihistamines removed from marketing due to associations with Torsades de Pointes and sudden death).

However, there are two issues that remain less than fully resolved. The first is a recent

report from Swedish authorities, shared with FDA, that they have identified an increased odds ratio for the occurrence of hypospadias (mislocation of the urethral opening in the penis) in association with loratadine use during pregnancy. However, checks of the US databases did not confirm such a signal here and preclinical data do not suggest that loratadine has such a propensity or even would likely do so based on pharmacology. Therefore, the conclusion of the reviewers in ODE II and in the Office of Drug Safety is that though there remains a small signal of concern over hypospadias that needs to be monitored and further considered, this signal is not sufficient to act on at this point and does not impact on the decision of whether this drug can be marketed OTC or not. The sponsor was asked and agreed to provide periodic updates specifically related to this issue as a post-marketing agreement.

The second issue is that the loratadine syrup was only recently approved for use in the 2 – 5 year old population. This approval was based on data obtained as a part of a written request (exclusivity has been granted for performance of the studies required under the written request). This dataset included PK data and a safety study for 2 weeks. In these studies, only approximately 125 children were studied. While there is no particular reason to be concerned about the safety of this drug in the 2 – 5 year old population, there remains little controlled data and limited post-marketing data to fully assess that there is an absence of any important differences compared to older children or adults. Given that loratadine has a very good safety profile, given the pediatric studies done to date and given that other antihistamines are used OTC in this age range, approving the drug down to age 2 in the syrup formulation appears reasonable. Note that for the tablets, Redi-tabs and the combination products, the dose is not appropriate for these children and therefore this issue/approval only pertains to the syrup. However, it also appears reasonable to have the sponsor specifically focus on children below the age of 6 years in their periodic safety update reports so that we can gain additional reassurance that no surprising safety issues are arising. The sponsor has agreed to do so.

Labeling:
The labeling review is largely the purview of DOTCDP. The reviewers in OTC have worked with the sponsor of this product (and competing 505(b)(2) products) to achieve consistent, clear, appropriate labeling. Particularly, I believe that DOTCDP has achieved a reasonable balance of describing this drug as relatively non-sedating in consumer appropriate ways. Since the labeling is largely derived from the monograph labeling for antihistamines, no labeling comprehension studies were required of the sponsor for the allergic rhinitis indication. These reviewers on 11/15/02 deemed the final draft labeling from the sponsor acceptable.

ACTION:

On behalf of ODE II, I offer the finding that these supplements, as amended, that propose the marketing of the loratadine line of products OTC for the treatment of hay fever and other upper respiratory allergies should be approved. I believe that such availability will provide an important choice for consumers who self-medicate for hay fever and other such allergies, particularly since loratadine is less sedating and therefore likely less impairing of driving than the currently available OTC choices.

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/s/

Robert Meyer
11/22/02 10:14:40 AM
MEDICAL OFFICER

RECORD OF TELEPHONE CONVERSATION

Date: October 31, 2002
Project Manager: Elaine Abraham
Subject: Preliminary labeling comments
NDA: Various supplements
Sponsor: Schering-Plough Corp.
Product Name: Claritin (Loratadine)
Phone No: (908) 740-5693

FDA participants: Marina Chang, R.Ph., Team Leader
Elaine Abraham, R.Ph., Project Manager

Schering participant: Mary Jane Boyle, Regulatory Affairs

Background: Schering-Plough submitted revised labeling dated October 24, 2002 for five efficacy supplements based on FDA's faxes of labeling comments sent earlier in the month. FDA called the sponsor with comments on the labeling.

Discussion: FDA provided the following preliminary comments on the labeling:

19-658 (S-018) Claritin (loratadine tablets, 10 mg)

5, 10, 20, and 40 Count Carton Labels

Under ***Questions*** subheading, the word "or" should not appear in bold typeface, but should appear in plain text font.

500 Count Carton Label

- ***Purpose*** subheading must be right justified according to 21 CFR 201.66(d)(6).
- Format Specifications
    a. Submit font sizes for ***Drug Facts*** and ***Drug Facts (continued)*** titles. According to 21 CFR 201.66(d)(2), the font sizes must be at least 9 point and 8 point, respectively.
    b. The heading font size must be increased from 7 point to 8 point as required by 21 CFR 201.66(d)(2).

c. Leading must be increased from 0 point to 0.5 point as required by 21 CFR 201.66(d)(3).

20-641 (S-009) Children's Claritin Syrup (1 mg/ml loratadine)

The Drug Facts panel on the carton label should be revised as follows:

20-704 (S-008) Claritin Reditabs (10 mg loratadine)

Revise the 4 and 10 count carton labels as follows:

Top and Bottom Panels

Rewrite the declaration of net quantity of contents (i.e., "Tablets") as "Orally Disintegrating Tablets" to accurately reflect the dosage form.

Back Panel

On the 10 count package label, rewrite the declaration of net quantity of contents (i.e., "Tablets") as "Orally Disintegrating Tablets" to accurately reflect the dosage form.

Back Panel: Drug Facts Panel

Under Directions, remove the propietary name "Reditabs®" because the agency generally does not permit propietary names to appear within the Drug Facts panel. In addition, the Active ingredient heading defines the dosage form within the Drug Facts panel as "tablet" not as "Reditabs® tablet".

19-670 (S-018) Claritin-D® 12 Hour Extended Release Tablets
and
20-470 (S-016) Claritin-D® 24 Hour Extended Release Tablets

Revise the Drug Facts panel on 10 and 20 count carton labels as follows:

- Leading must be increased from 0 point to 0.5 point as required by 21 CFR 201.66(d)(3).

FDA recommended that the labeling be revised with the above changes and submitted to the NDA as a minor labeling amendment. They will submit the — count size when they submit the revised labeling.

Draft by: HFD-560/Abraham/10-31-02
OK: HFD-560/Chang/11-1-02

C:\word\Claritin Labeling Tcon.doc

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

FACSIMILE TRANSMITTAL SHEET

DATE: October 4, 2002

To: Ms. Mary Jane Boyle	**From: Anthony Zeccola**
Company: Schering Corporation	Division of Pulmonary and Allergy Drug Products
Fax number: 908-740-4131	**Fax number:** 301-827-1271
Phone number:	**Phone number:** 301-827-1058

Subject: NDA 20-470

Total no. of pages including cover: 4 (Including electronic signature page)

Comments: As Discussued

Document to be mailed: ☐YES ☑NO

Mary Jane,

As discussed during our telephone conversation, here are the Agency's revisions to the Claritin OTC labeling for NDA 20-470 for Claritin-D 24 Hour (loratadine 10 mg/pseudoephedrine 240 mg) Extended Release Tablets.

Please note that we cannot review and comment on labeling 5-count packages until you submit such labeling, therefore the following comments pertain to the 10-count carton and 10-count blister pack labels. Please submit revised labeling incorporating the following comments.

10 Count Carton Label

1. Principal Display Panel

   a. Reword the phrase ——Prescription Strength" to "Original Prescription Strength."

   b. Add an asterisk ("*") following the phrase "Non-Drowsy." In addition, the following statement must appear at the bottom of the PDP in conspicuous print: "*When taken as directed. See Drug Facts Panel."
   c. Delete "24 hour" in the statement "24 hour Extended Release Tablets" to avoid redundancy on the PDP.

   d. Amend the declaration of contents to read " 10 Extended Release Tablets" so that entire dosage form is listed.

2. Top Panel

   Add an asterisk ("*") following the phrase "Non-Drowsy." Add the statement in conspicuous print: "*When taken as directed. See Drug Facts Panel." See 1b, above for discussion.

3. Bottom Panel and Flaps

   Add an asterisk ("*") following the phrase "Non-Drowsy." Add the statement in conspicuous print: "*When taken as directed. See Drug Facts Panel." See 1b, above for discussion.

4. Back Panel

   a. Add an asterisk ("*") following the phrase "Non-Drowsy." Add the statement in conspicuous print: "*When taken as directed. See Drug Facts Panel." See 1b, above for discussion.

   b. Drug Facts

   (1)

   (2)

   (3)

   (4) Bold entire statement under **When using this product** subheading as required by 21 CFR 314.80(c)(1)(ii)(A).

   (5) Revise directions by incorporating dosing information into a table as follows:

   • do not divide, crush, chew , or dissolve tablet

Adults and children 12 years and over	1 tablet daily with a full glass of water; not more than 1 tablet in 24 hours
Children under 12	Ask a doctor
Consumers with liver or kidney disease	Ask a doctor

   (6) Debold "or" between phone number and website URL under ***Questions?*** Heading.

10 Count Blister Pack Label

5. Add the dosage form "Extended Release Tablet" to the label.

Memorandum of Internal Meeting Minutes

MEETING DATE: October 4, 2002

TIME: 11:00AM

LOCATION: 10B45 Conference Room

APPLICATION: NDA 19-658

Division of Pulmonary and Allergy Drug Products Participants:

Badrul Chowdhury, M.D., Ph.D., Acting Division Director
Charles Lee, M.D., Medical Officer
Mary Purker, M.D., Ph.D., Medical Team Leader
Larry Sancilio, Ph.D., Pharmacology/Toxicology Reviewer
Joseph Sun, Ph.D., Pharmacology/Toxicology Team Leader
Anthony M. Zeccola, Regulatory Management Officer

Division of Over-the-Counter Drug Products Participants:

Matthew Holman, Ph.D., Labeling Reviewer
Linda Hu, M.D., Medical Officer
Cazemiro Martin, Ph.D., Chemist

Office of Drug Safety Participants:

Allen Brinker, M.D., M.S, Medical Team Leader
Carolyn McCloskey, M.D., M.P.H., Medical Officer
Quynh Nguyen, Pharm.D., Regulatory Health Project Manager

Background: This meeting was called in response to reports in the Swedish Birth Registry of hypospadias births that possibly could be associated with the maternal use of loratadine. Following receipt of these reports, the Agency sent a request to Schering Corporation for an assessment of all data that they have on this subject. Independent of Schering's assessment, the Agency initiated its' own assessment of the data available. The Agency's evaluation, based on all currently available hypospadias reports, as well as results from animal studies conducted by Schering Corporation, was conducted by medical and pharmacology/toxicology staff members from the Division of Pulmonary and Allergy Drug Products, the Office of Drug Safety, as well as Dr. Scialli's, a Special Government Employee from Georgetown University. In addition, the Agency has solicited input from epidemiologists from the Centers for Disease Control and Prevention (CDC), based on any additional data that they might have access to, however the CDC report was not available at the time of this meeting.

Discussion

1. Overview of the Swedish Data Results that Precipitated this meeting (see Attachment 1, Lee)

2. Overview of Dr. Scialli's Comments Regarding Pharmacology/ Toxicology Concerns and FDA Response to those Concerns. DPADP toxicologists reviewed animal study data for both Clarinex and Claritin (See Attachment 2, Sancilio).

3. Overview of Dr. Scialli's Assessment of the Swedish Birth Registry Epidemiologic Data and FDA's Response. ODS reviewed the Swedish data in light of Dr. Scialli's comments and discussed their view of the data. The ODS impression is that there is clearly a signal, but a strong recommendation cannot be made at this time, in the absence of additional data from other geographic areas. The latest additional AERS reports, most of which are US cases in response to the media reports on the Swedish study, do not add new information on this issue.

4. Group Discussion about the Regulatory Path Forward.

   a. What actions are the Swedes taking as a result of these data?
   At this point, it appears that the Swedes have not taken any action as a result of these reports other then to report them to the European Union regulatory authorities. The EMEA (European regulatory authority) had scheduled a meeting similar in purpose to this meeting, but have postponed it until some time in October 2002 although at this time, we are not aware of the exact date.

   b. It was agreed that while the Swedish Birth Registry database is an excellent source of epidemiologic data, these reports still constitute a small number of cases, especially in light of the twin case and the two to four cases with indeterminate time; duration and level of exposure . Furthermore, the severity of the cases were not different in the claritin exposed children than those not exposed to claritin in utero.

   c. Given a. and b. above, should the labels for loratadine products be modified at this time?
   In light of 3. above, the labels need not be modified at this time, instead it was agreed that we should discuss the possibility of a Phase IV (postmarketing) study on the part of Schering Corporation. This study would likely take the form of an epidemiologic study, the purpose of which would be to review all available data over the next three years.

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/s/

Anthony Zeccola
11/25/02 01:08:31 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

560-3228 **REQUEST FOR CONSULTATION**

TO *(Division/Office)*:	FROM:
Karen Lechter, OPSS/DSRCS, HFD-410	Charles J. Ganley, M.D., Director, DOTCDP, HFD-560

DATE	IND NO.	NDA NO. : 19-658, 20-704 and 20-641	TYPE OF DOCUMENT: Label comprehension study report 1.0	DATE OF DOCUMENT: 9/25/02
October 3, 2002				

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Claritin	HIGH	Antihistamine (hives relief)	10/31/02

NAME OF FIRM: Schering-Plough

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- X OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Please review the label comprehension study report and provide your comments. If you have any questions, you can call Linda Hu at 301/827-2267 or Elaine Abraham at 301/827-2301.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
/S/	☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

FACSIMILE TRANSMITTAL SHEET

DATE: September 27, 2002

To: Ms. Mary Jane Boyle	**From: Anthony Zeccola**
Company: Schering Corporation	Division of Pulmonary and Allergy Drug Products
Fax number: 908-740-4131	**Fax number:** 301-827-1271
Phone number:	**Phone number:** 301-827-1058

Subject: NDA 19-658

Total no. of pages including cover: 4 (Including electronic signature page)

Comments: As Discussued

Document to be mailed: ☐YES ☑NO

Mary Jane,

As discussed during our telephone conversation, here are the Agency's revisions to the Claritin OTC labeling for NDA 19-658 for Claritin 10mg tablets.

Please note that we cannot review and comment on labeling for the 2, 10, 20, or 40-count packages until you submit such labeling, therefore the following comments pertain to the 5-count carton label. Please submit revised labeling incorporating the following comments.

1. Principal Display Panel

   a. Reword the phrase ' —— Prescription Strength" to "Original Prescription Strength." We reviewed your justification for not revising the statement. We recognize the examples of OTC drug products using the proposed phrase. We agree that consumers should understand that OTC Claritin is the same dosage strength as prescription Claritin. Using the word "Original" should prevent consumer confusion about the dosage strength and may deter the use of OTC Claritin for the treatment of hives.

   b. Add an asterisk ("*") following the phrase "Non-Drowsy." In addition, the following statement must appear at the bottom of the PDP in conspicuous print: "*When taken as directed. See Drug Facts Panel." We reviewed your argument against this change; however, we have determined that this labeling is to be included on all OTC loratadine drug products to ensure that consumers understand that drowsiness may result at dosages above 10 mg daily.

2. Top Panel

   Add an asterisk ("*") following the phrase "Non-Drowsy." Add the statement in conspicuous print "*When taken as directed. See Drug Facts Panel." See 1.b. above for explanation.

3. Bottom Panel and Flaps

   Add an asterisk ("*") following the phrase "Non-Drowsy." Add the statement in conspicuous print "*When taken as directed. See Drug Facts Panel.", if space allows.

4. Back Panel

   a. Add an asterisk ("*") following the phrase "Non-Drowsy." Add the statement in conspicuous print "*When taken as directed. See Drug Facts Panel." See 1.b above for explanation.

b. [redacted]

c. Add directions for individuals with liver or kidney disease to the directions listed in a table as shown below:

Adults and children 6 years and over	1 tablet daily; not more than 1 tablet in 24 hours
Children under 6	Ask a doctor
Consumers with liver or kidney disease	Ask a doctor

You may be correct in asserting that there are not specific doses for consumers with liver or kidney disease; however, in the prescription labeling, there is a recommended dose adjustment for these patients. Thus, the OTC label must include directions for consumers with liver or kidney disease. This direction reiterates the point that these consumers can take the product, but only after consulting a physician.

d. Remove bold typeface from "or" in the *Questions?* heading.

5. 5-Count Blister Pack Label

[redacted]

6. 10-Count Blister Pack

a. Include the dosage form (tablet) on the label.

b. Include "Dist. By" as it appears on the 5-count blister pack label. The label should bear the name and place of business, in accordance with 21 CFR 201.1.

7. We recommend that you increase font size and change font color to accentuate contrast with the background, and that you make indications more conspicuous on PDP.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-470/S-019

CBE SUPPLEMENT

Schering Corporation
Attention: Mary Jane Nehring,
Senior Director, Marketed Products Support and Training
2000 Galloping Hill Rd
Kenilworth, NJ 07033

Dear Ms. Nehring:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Claritin-D 24 Hour (10 mg loratadine and 240 mg pseudoephedrine sulfate) Extended Release Tablets

NDA Number: 20-470

Supplement number: 019

Date of supplement: February 10, 2003

Date of receipt: February 11, 2003

This supplemental application, submitted as "Supplement - Changes Being Effected" provides a change in the labeled storage conditions for Claritin-D 24 Hour Tablets.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on April 12, 2003 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be August 10, 2003.

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service:
Center for Drug Evaluation and Research
Division of Over-the-Counter Drug Products, HFD-560
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5600 Fishers Lane
Rockville, Maryland 20857

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Rockville, Maryland 20850-3202

If you have any questions, call Elaine Abraham, Regulatory Project Manager, at (301) 827-2301.

Sincerely,

{See appended electronic signature page}

David Hilfiker
Chief, Project Management Staff
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research